wherein said low-molecular weight peptides, used for said measurement have a molecular weight of not more than 30,000 Dalton;

directly detecting said low molecular weight peptides by mass spectrometry; and

relating said low-molecular weight peptides to a reference; and

said reference comprises a distribution of low-molecular weight peptides in a representative cross-section of defined controls to produce a differential peptide display.

REMARKS

Reconsideration of this patent application is respectfully requested in view of the foregoing amendments, and the following remarks.

The amendments to the claims are as follows. Claim 1 has been amended to recite that the "sample" is limited to "a body fluid sample from the organism selected from the group consisting

of hemofiltrate, ascitic fluid and urine". Also the "organism" is selected from the group consisting of "animals and humans." The objected to terminology "substantially the entirety of" and the objected to terminology "substantially of the detected" have been deleted.

In claim 1, it has been stated that directly detecting said low molecular weight peptides is "by MALDI mass spectrometry."

In amended claim 1, the phrase "wherein the detecting of said low molecular weight peptides is effected by parameters such as molecular weight" has been canceled. This is because claim 1 is specifying that the detecting is by "MALDI". Newly added claim 14 recites all the features of amended claim 1, except that the step of "directly detecting said low molecular weight peptides" is by "chromatography", rather than by MALDI.

Newly added claim 15 recites all of the features of amended claim 1, except that the body fluid sample Markush group also includes blood and except that the step of directly detecting of

low molecular weight peptides is by mass spectrometry.

The rejections under 35 U.S.C. 112, first paragraph and second paragraph were maintained for the reasons of record as set forth in the previous office action. The Patent Examiner has argued as follows:

Applicant states that the self explanatory Declaration of Dr. Schulz-Knappe answers the enablement and second paragraph issues. However, the Patent Examiner finds that the Declaration of Dr. Schulz-Knappe explains the general use of the various terminologies used in the field but does not show support for the enablement issues raised by the Office Action especially a method for detecting pathogenic and non-pathogenic status in a given sample. Applicant gives explanation of various issues raised under 112, second paragraph. Such explanation is not supported by the claims. In other word, applicant is arguing the limitations, which are not present in the claim. For example; Applicant explains the "condition of organism" can be good or bad. However, this method is to detect a pathogenic or any other

condition of an organism. First of all "organism" could include E. coli. which indicates the "normal condition" of bacteria. The Patent Examiner has thusly questioned, what is the pathogenic condition of an E. coli?

The Patent Examiner has stated that "organism" includes, per se a virus, therefore, what is the pathogenic condition of a virus? And what are the combinations? The Patent Examiner has questioned that if "organism" reads on using an intact and complete animal such as human, then how is such an organism detected by this method?

Further, it is not clear how low molecular weight peptide define the pathogenic condition directly? The term "such as" renders the claim indefinite. Similarly the terms "reference", "representative" "defined controls" and "peptide display" are confusing.

In answer to these objections, the above-discussed amendments to the claims have canceled all of these objected-to-

terms.

The Patent Examiner has also contended as follows.

The amendment filed 1/7/02 was objected to under 35 U.S.C. 132 because it allegedly introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which allegedly is not supported by the original disclosure is as follows: claim 1, "substantially the entirety" and "substantially of the detected".

Claims 1, 4-9 and 11-13 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the recitation of "substantially the entirety" and "substantially of the detected" in claim 1.

Claim 1 was objected to because of the following informalities: "procaryote", and "eucaryote" are not correct. Claim 1 was rejected as being vague and indefinite for the recitation of "substantially". Claim 1 is confusing for the recitation of "substantially of the detected".

In response thereto, the above-discussed amendments to the claims have canceled all of this objected-to terminology.

The description and the claims provide a sufficient disclosure as follows for the present invention. In a first step, the present invention comprises the analytical step, i.e., preparation of a sample and measurement of the peptides.

In preferred embodiments, the analysis is performed by mass spectroscopy (see page 3, last paragraph). MALDI and ESI mass spectrometry are especially mentioned on page 7, paragraph 3. A further possibility for measuring the peptides is analysis on chromatographic columns. Whereas mass spectrometry measures the weight or the weight/charge ratio, chromatography may measure

different characteristics depending on the type of chromatographic support.

After analysis, a "peptide profile" being specific for the respective sample is generated.

In a further step, the invention provides a method for detecting the condition of the sample or the organism from which the sample is derived. This is done by comparing the peptide profile to a reference peptide profile.

The reference peptide profile can be similar samples or organisms. Therefore one skilled in the art can

(a) identify peptides which are relevant for a certain condition, for example by comparing peptides of a pregnant woman with a reference profile from a non-pregnant woman or,

(b) if one is aware of the relevant peptides, one can identify (diagnose) a certain condition by, for example,

comparing a peptide profile of a woman with a reference peptide profile from pregnant women and a reference profile from non-pregnant woman.

By comparing with the respective reference profiles, it is possible by the present method to diagnose all kinds of conditions or diseases.

If the sample is a cell culture or bacteria, it would be difficult to identify "normal" or "pathological" states but one can always identify differences, for example of cell cultures before and after treatment with a substance or between similar strains of the same bacteria.

The above-noted amendments to the claims are based upon the following information. The Patent Examiner has stated, on page 3 of the April 24, 2001 Office Action, that the present Specification "while being enabling for a method of detecting the low molecular weight peptides by so-called MALDI method does not reasonably provide enablement for any other method."

In the paragraph bridging pages 3-4 of the Office Action dated April 24, 2001, the Patent Examiner has stated that "in the instant case, other than a method for determining the low molecular weight peptides by so-called MALDI method from body fluids such as hemofiltrate, ascitic fluid and urine, the instant specification is not enabled." Again, the Patent Examiner has stated in the same paragraph, "Specification provides guidance and direction to a method for determining the low molecular weight peptides by so-called MALDI method from body fluids such as hemofiltrate, ascitic fluid and urine (specification pages 8 to 15)."

For all these reasons, it is firmly believed that all the claims are now in complete compliance with the requirements of 35 U.S.C. 112 and 35 U.S.C. 132. Withdrawal of these grounds of rejection is respectfully requested.

Concerning newly added claim 15, according to the amended claims, the sample is a body fluid sample selected from the group consisting of hemofiltrate, ascitic fluid and urine. The most

common sample for diagnostic purposes is blood. Thus blood is included in the "body fluid samples" of the claims. Blood samples are not mentioned in the application text but on page 3, second paragraph "fluid samples from organism" are mentioned. Fluid samples from organism such as humans and animals are most commonly blood samples. After removal of the cell compounds, plasma is obtained which is the usual diagnostic sample.

Treatment of such a sample is described on page 5, last paragraph to third paragraph of page 7 of the present Specification.

This way of preparing a sample blood is simple, the product is comparable to hemofiltrate (also called blood filtrate) described in example 1, which is a diluted blood extract from patients suffering from a chronical renal disease.

Mass spectrometry is one of the preferred ways of measuring the peptides. There are several ionization methods for measuring peptides by mass spectrometry for example MALDI (Matrix Assisted

Disorption Ionization) and ESI (Electro Spray Ionization). These two methods are mentioned on page 7, third paragraph. Ionization methods for measuring peptides were known at the filing date of the present invention. Thus the measuring method recited by claim 15 is by "...directly detecting said low molecular weight peptides by mass spectrometry..."

The rejection of claims 1, 4, 8, 12 and 13 under 35 U.S.C. 102(b) as being anticipated by *Harry et al, 1989* (Clinical Microbiology Reviews, Vol. 2, pages 241-249) is traversed.

The rejection of claims 1, 4, 8 under U.S.C. 102(b) as being anticipated by *Ausubel et al 1995* (Short Protocols In Molecular Biology, Chapter on analysis of proteins) is traversed.

The rejection of claims 1, 4-9, and 11-13 under 35 U.S.C. 102(b) as being anticipated by *Jimenez et al 1994* (Journal of Neurochemistry; Vol. 62; pages 404-407) is traversed.

None of these references teach a method comprising the following steps:

taking a sample, and said sample being a body fluid sample from said organism selected from the group consisting of hemofiltrate, ascitic fluid and urine;

wherein said organism is selected from the group consisting of animals and humans;

measuring peptides from said sample of said organism containing high-molecular weight peptides and low-molecular weight peptides, as an indication of the pathogenic or any other condition of said organism;

wherein said low-molecular weight peptides, used for said measurement have a molecular weight of not more than 30,000 Dalton;

directly detecting said low molecular weight peptides by MALDI mass spectrometry; and

relating said low-molecular weight peptides to a reference; and

said reference comprises a distribution of low-molecular weight peptides in a representative cross-section of

defined controls to produce a differential peptide display.

None of these references teach or suggest all of the steps now specified by amended claim 1 or by newly added claims 14 or 15. Thus there can be no anticipation under 35 U.S.C. 102. Withdrawal of this ground of rejection is respectfully requested.

In addition, none of these prior art references disclose the present invention under 35 U.S.C. 103.

A prompt notification of allowability is respectfully requested.

Respectfully submitted,
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Enclosures:
(1) Marked-Up Version of Amended Claim;
(2) Copy of One Month Extension of Time; check for $55.00.

I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to: Assistant Commissioner of Patents, Washington, D.C. 20231, on July 22, 2002.

Ingrid Mittendorf

MARKED-UP VERSION
OF
AMENDED CLAIM

1. (Four Times Amended). A method for detecting a pathogenic or any other condition of an organism comprising the steps of

taking a sample, and said sample <u>being</u> [is selected from the group consisting of a tissue sample,] a <u>body</u> fluid sample from said organism[, the organism itself, the combinations thereof; and] <u>selected from the group consisting of hemofiltrate, ascitic fluid and urine;</u>

wherein said organism is selected from the group consisting of [a procarvote, a eucarvote, a multicellular organism, cells from tissue cultures, and cells from] animals and humans;

measuring [substantially the entirety of] peptides from said sample of said organism containing high-molecular weight peptides and low-molecular weight peptides, as an indication of the pathogenic or any other condition of said organism;

wherein said low-molecular weight peptides, used for said measurement have a molecular weight of not more than 30,000 Dalton;

directly detecting said low molecular weight peptides

by MALDI mass spectrometry; and

[wherein the detecting of said low-molecular weight peptides is effected by parameters such as molecular weight;]

relating [substantially of the detected] said low-molecular weight peptides to a reference; and

said reference comprises a distribution of low-molecular weight peptides in a representative cross-section of defined controls to produce a differential peptide display.